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Preparation and nickel-catalyzed coupling reactions of divinylic selenides

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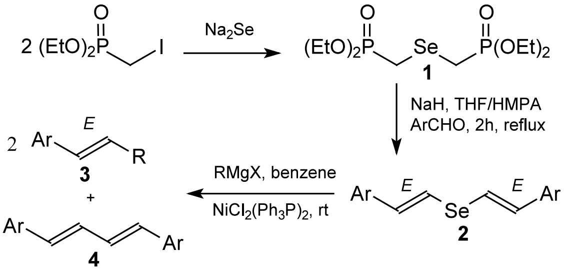
Abstract—The preparation of divinylic selenides by the reaction of selenium bis-phosphonate with aromatic aldehydes is described. The nickel-catalyzed cross coupling of the divinylic selenides with Grignard reagents was also studied. © 2002 Elsevier Science Ltd. All rights reserved.

Vinylic selenides are useful intermediates for the synthesis of several compounds and much attention has been devoted to their preparation and to their synthetic utilization.[1] From the several methods for the synthesis of vinylic selenides, the Wittig or Wittig–Horner reactions constitute one of the most useful.[2] We have recently reported convenient methods for the synthesis of vinylic selenides by Wittig or Wittig–Horner routes.[3]

From the many applications of this class of compounds, the cross coupling reaction with Grignard reagents catalyzed by Ni(II) constitutes one of the most useful. The reaction of vinylic selenides with PhMgBr and *n*-BuMgBr, catalyzed by $NiCl_2(Ph_3P)_2$ or $Ni(dppp)Cl_2$, to give the corresponding cross-coupling products has been described. These reactions proceeded with retention of configuration and in good yields.[4] A chemoselective coupling reaction was described by the reaction of (*E*)- and (*Z*)-(phenylthio)ethenyl methyl selenides with Grignard reagents, catalyzed by Ni(II) species, in which only the selenium organyl is removed. The stereospecific carbon–selenium bond cleavage can be achieved by the choice of the appropriate Ni catalyst.[5] The coupling of vinylic selenides has also been applied to the synthesis of allyl silanes by reaction with trimethylsilylmagnesium chloride and $NiCl_2(Ph_3P)_2$ or $PdCl_2(Ph_3P)_2$ catalysis.[6] However, in all these methods, when the coupling reaction is performed, one of the two organic moieties linked to the selenium atom, which is usually a phenyl or a methyl group, is lost. In this way, we envisioned that by using divinylic selenides on these coupling reactions, both organyls linked to selenium could eventually be transferred. A search on the literature shows that divinylic selenides have been prepared by the reaction of vinyl selenide anions with (*E*)- or (*Z*)-β-bromo styrenes.[7] The vinyl selenide anions were generated in situ by the cleavage of methylselenium styryls with lithium methyl selenide anion in DMF or with sodium in DMA.[7] By this route, *E*/*E*-, *E*/*Z*- or *Z*/*Z*-bis-styryl selenides could be accessible, although in moderate yields. *Z*,*Z*-Distyryl selenide has also been prepared by reacting potassium diselenide and phenylacetylene in 82% yield.[8] However, the synthesis of divinylic selenides by the Wittig–Horner route has not been properly studied, since only one example was described,[9] by the reaction of the corresponding selenium bis-phosphonate **1** with benzaldehyde, Scheme 1. In this way, we decided to explore the full scope of this method and the application of the prepared divinylic selenides in the cross-coupling reaction with Grignard reagents catalyzed by Ni(II)-phosphines, as presented in Scheme 1.



Scheme 1.

Keywords: coupling reactions; nickel and compounds; selenium and compounds; vinylic selenides.

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For the synthesis of divinylic selenides by the Wittig–Horner route, the first step was the preparation of the selenium bis-phosphonate **1**. This intermediate was obtained in 71% isolated yield by the addition of a THF solution of the iodomethylphosphonate to Na_2Se (conveniently generated in situ by the reduction of selenium with $NaBH_4$ in ethyl alcohol),[10] followed by 2 h at reflux.[11] The preparation of the divinylic selenides **2a**–**g** was performed by treatment of the bis-phosphonate **1** with NaH as a base, in THF, followed by the addition of the appropriate aryl aldehyde, according to Scheme 1. The results of this reaction are summarized in Table 1. In some examples good results could only be obtained by the use of HMPA as a co-solvent.[12] Unfortunately, the reaction was successful only to aromatic aldehydes. ^1H NMR analysis indicated the almost exclusive formation of the (*E*,*E*)-isomers in all examples studied. In some examples, a very small amount of *Z*-isomer could be detected by ^1H and ^{13}C NMR, easily removed by column chromatography or during recrystallization.

Table 1. Divinylic selenides **2a**–**g** prepared according to Scheme 1

Entry	Aldehyde	Product	Yield (%)[a]	Mp (°C)[c,d]
1	C_6H_5CHO	**2a**	75[b]	45–47
2	3,4-OCH_2O-C_6H_3CHO	**2b**	87[b]	88–90
3	4-CH_3O-C_6H_4CHO	**2c**	54	106–108
4	3,4-Di-(CH_3O)-C_6H_3CHO	**2d**	72[b]	93–95
5	$C_6H_5CH{=}CHCHO$	**2e**	61[b]	86–87
6	4-Cl-C_6H_4CHO	**2f**	53[b]	126–128
7	4-CH_3-C_6H_4CHO	**2g**	51	74–76

[a] Isolated yields after column chromatography.
[b] HMPA (0.5–1 mL) used as co-solvent.
[c] From hexane.
[d] All products were fully characterized by spectroscopic methods.

The next step was the cross-coupling reaction of divinylic selenides with Grignard reagents to find out if the behavior of these species would be the same as a normal vinylic selenide and if both styryl groups could be transferred to the product. We started trying the reaction of distyryl selenide **2a** with PhMgBr in a reaction catalyzed by $NiCl_2(Ph_3P)_2$ in benzene as the solvent. Using 10 mol% of catalyst, total consumption of the starting material was observed (although 5 mol% or less are also equally effective), and the product was isolated in 62% yield (entry 1, Table 2), along with 35% of the 1,4-diphenyl butadiene. A quite different behavior was observed in the reaction of **2a** with $C_8H_{17}MgBr$, since an incomplete reaction occurred and the desired product was isolated in low yield. Total disappearance (as judged by TLC) of **2a** was observed using an equimolar amount of the catalyst after 3 h of reaction, at room temperature, and the corresponding product **3a** was isolated after column chromatography in 63% yield.[12] However, we observed that, by using 1 equiv. of LiCl, the reaction could be performed to completion using 10 mol% of $NiCl_2(Ph_3P)_2$, and the product was isolated in 68% yield. As we expected, we were able to transfer to the product both organyls linked to the selenium atom, which is removed at the end of the reaction as black selenium by filtration in Celite. The reaction was then extended to some other bis-vinylic selenides **2c** and **2g**. In all cases, moderate to good yields of the desired products **3a**–**f** were isolated, but the formation of the 1,4-diaryl-1,3-butadienes could not be avoided, even after several modifications that we made in the experimental procedure (Table 2). Fortunately, these species can be very easily removed by column chromatography (see experimental).[13] As expected, in all these coupling reactions, only *E*-vinylic products were obtained.

In summary, we describe a convenient preparation of divinylic selenides by a Wittig–Horner route and observe that these species participate conveniently in nickel-catalyzed cross-coupling reactions with Grignard reagents, with total retention of configuration.

Table 2. Cross-coupling products **3** prepared according to Scheme 1

Entry	Ar	R	**3**			Yield **4** (%)
				Yield (%)	Mp (°C)	
1	C_6H_5	C_6H_5	**3a**	62	122–124[a]	35
2	C_6H_5	C_8H_{17}	**3b**	68	–[b]	23
3	4-$CH_3C_6H_4$	C_6H_5	**3c**	56	117–119[c]	24
4	4-$CH_3C_6H_4$	C_8H_{17}	**3d**	59	–[b]	18
5	4-$CH_3OC_6H_4$	C_6H_5	**3e**	86	133–135[d]	10
6	4-$CH_3OC_6H_4$	C_8H_{17}	**3f**	62	–[b]	12

[a] Mp 123–124°C.[14]
[b] Oil.
[c] Mp 116–118°C.[15]
[d] Mp 135°C.[15]

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10. This reagent, although commercially available from Alfa Aesar, it is moisture sensitive and quite expensive.
11. *Preparation of the selenium bis-phosphonate **1***:[9] In a 100 mL round-bottom flask equipped with an addition funnel and reflux condenser under argon charged with selenium (1.11 g, 14 mmol) and absolute ethyl alcohol (40 ml) was added dropwise a solution of $NaBH_4$ (1.26 g, 33 mmol) in water (10 ml). After the addition of reagents was complete, the mixture was refluxed until the dissolution of selenium was complete. The solution was cooled to room temperature and a solution of the iodomethyl(diethylphosphonate) (7.78 g, 28 mmol) in THF (40 ml) was added. The mixture was refluxed for 2 h, cooled to room temperature, water was added and then extracted with ethyl acetate. The organics were washed with an aqueous saturated solution of NH_4Cl, dried over $MgSO_4$ and the solvent removed under vacuum. The residue was purified by column chromatography, eluting with hexane/ethyl acetate (7:3) or vacuum distillation (bp 250°C/0.5 mmHg). Yield: 3.78 g, 71%.
12. *General procedure for the preparation of the divinylic selenides **2***: To a 25 ml round-bottom flask, under argon and equipped with a reflux condenser, was added THF (5 mL), NaH (0.060 g, 2.4 mmol), a solution of the selenium bis-phosphonate **1** (0.45 g, 1.2 mmol) in THF (4 mL) and after 10 min the aldehyde (2 mmol) and HMPA (0.5–1 mL; see text and Table 1). The reaction mixture was refluxed for 2 h, cooled to room temperature, water was added and extracted with ethyl acetate, the organics dried over $MgSO_4$ and the solvent was removed under vacuum. The residue was purified by silica gel column chromatography, eluting with hexane or mixtures of hexane/ethyl acetate. Selected spectroscopic data. Compound **2a**:[9] ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.86 (d, 2H, $J=15.8$ Hz), 7.11 (d, 2H, $J=15.8$ Hz), 7.20–7.40 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 117.7, 125.9, 127.6, 128.6, 134.7, 136.9; GC/MS m/z 286 (M^++1, 9%), 205, 190, 128, 102, 76 (100%). Compound **2c**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.80 (s, 6H), 6.81 (d, 2H, $J=15.8$ Hz), 6.85 (d, 4H, $J=8.7$ Hz), 6.96 (d, 2H, $J=15.8$ Hz), 7.28 (d, 4H, $J=8.6$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 55.3, 114.1, 114.9, 127.3, 130.0, 134.7, 159.3; GC/MS m/z 344 (M^++1, 2.4%), 266 (100%), 251, 235, 220, 207, 158, 134, 121, 91. Compound **2f**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.81 (d, 2H, $J=15.8$ Hz), 7.11 (d, 2H, $J=15.8$ Hz), 7.20–7.35 (m, 8H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 118.3, 127.2, 128.9, 133.4, 133.6, 135.3; GC/MS m/z 354 (M^+, 3%), 274, 239, 204, 127, 101 (100%), 75. Compound **2g**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.33 (s, 6H), 6.84 (d, 2H, $J=16$ Hz), 7.07 (d, 2H, $J=16$ Hz), 7.13 (d, 4H, $J=8$ Hz), 7.23 (d, 4H, $J=8$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 21.2, 116.2, 125.9, 129.3, 134.2, 134.4, 137.5; GC/MS m/z 314 (M^++1, 9.6%), 234, 219, 203, 115 (100%), 105, 91.
13. *General procedure for the coupling reaction. Preparation of **3b***: To a 25 mL flask under argon was added the catalyst [$NiCl_2(PPh_3)_2$; 0.035 g, 0.05 mmol)], LiCl (0.021 g, 0.5 mmol; for aliphatic Grignard) and dry benzene (3 mL), followed by $C_8H_{17}MgBr$ (0.5 mL, 0.5 mmol, 1 M solution). After 15 min, more of the Grignard reagent (1.5 mL, 1.5 mmol) and **2a** (0.143 g, 0.5 mmol) in dry benzene (3 mL) was added. The reaction mixture became dark and was stirred for 3 h at rt, followed by the addition of water. The solids formed were filtered under Celite, washing with ethyl acetate. The organics were washed with an aqueous saturated solution of NH_4Cl, dried over $MgSO_4$, the solvent removed under vacuo and the residue was purified by silica gel column chromatography, using hexane as the eluent, first eluting the coupling product **3b** (1.146 g, 68% yield), followed by the butadiene. Selected spectroscopic data. Compound **3b**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.85–0.90 (m, 3H), 1.2–1.5 (m, 12H), 2.19 (q, 2H, $J=6.8$ Hz), 6.20 (dt, 1H, $J=15.8$ and 6.4 Hz), 6.38 (d, 1H, $J=15.8$ Hz), 7.10–7.40 (m, 5H) (data in accordance with Ref. 17); ^{13}C NMR (50 MHz, $CDCl_3$): δ 14.0, 22.6, 29.2, 29.3, 29.4, 29.5, 31.9, 33.0, 125.9, 126.7, 128.4, 129.7, 131.1, 137.9; IR (film, cm^{-1}) 2923, 2852, 1494, 1465; GC/MS m/z 216 (M^+, 14%), 117, 104, 71, 57, 43 (100%). (1*E*,3*E*)-1,4-Diphenyl-1,3-butadiene: mp 148–150°C (Lit.[16] mp 151–153°C). Compound **3c**: mp 117–119°C (Lit.[15] mp 116–118°C); ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.34 (s, 3H), 7.0–7.6 (m, 11H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 21.2, 126.4, 127.4, 127.7, 128.7, 129.4, 133.6, 137.5; GC/MS m/z 194 (M^+, 7%), 179, 115, 28 (100%); IR (KBr, cm^{-1}) 3022, 2914, 1593, 1509, 1466, 968. (1*E*,3*E*)-1,4-Di-*p*-tolyl-1,3-butadiene: mp 202–204°C. Compound **3e**: mp 133–135°C (Lit.[15] mp 135°C); ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.83 (s, 3H), 6.90 (d, 2H, $J=8.8$ Hz), 7.0–7.5 (m, 9H); ^{13}C NMR (50 MHz,

CDCl$_3$): δ 55.3, 114.1, 126.2, 127.1, 127.7, 128.2, 128.6, 130.1, 137.6, 159.3; GC/MS m/z 210 (M$^+$, 6%), 165, 152, 40, 28 (100%); IR (KBr, cm^{-1}) 2961, 1509, 1264, 1173, 1029. (1*E*,3*E*)-1,4-Di-*p*-anisoyl-1,3-butadiene: mp 221–223°C (Lit.[18] 224–226°C).

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